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PhRMA

March 19, 1999

Dockets Management Branch (HFA 305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, Maryland 20852

RE: Draft Guidance for Industry on Content and Format for Geriatric Labeling; Docket No. 98D-1169

Dear Sir/Madam:

The Pharmaceutical Research and Manufacturers of America (PhRMA) represents the country's leading research-based pharmaceutical and biotechnology companies, which are devoted to inventing medicines that allow patients to lead longer, happier, healthier and more productive lives. Investing over $24 billion annually in discovering and developing new medicines, PhRMA companies are leading the way in the search for cures. PhRMA is pleased to submit these comments on the Draft Guidance for Industry on Content and Format for Geriatric Labeling, Docket No. 98D-1169.

Label Changes Prior to FDA Approval – PhRMA notes that this Guidance provides direction to the industry on implementation dates and optional standard language for revised labeling to include additional information about the use of drugs and biological products in the elderly. The Guidance explicitly notes when sponsors may implement labeling changes without waiting for FDA approval, i.e., when the labeling change strengthens instructions for use or where insufficient information exists to determine whether geriatric patients' responses to use of a drug product differ from responses of non-geriatric patients.

Table of Submission Dates – In the Guidance, FDA presents a Table that sets forth the dates on which sponsors of drugs or biologics must submit proposed labeling changes, depending upon when FDA first approved the product. This summary of submission dates will be helpful to sponsors, particularly those with numerous products for which they must complete data compilation and review and submit proposed new labeling.

Source Data to Support Labeling Change – The Guidance states that the sponsor should submit the source data and the analysis to support any change in labeling. PhRMA notes that, in some instances, the source data may already have been submitted to FDA, i.e., when the data are from clinical studies used to support the

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original application, but the sponsor has reanalyzed those data to determine the effects of the drug on a subset of the clinical trial participants, the elderly. PhRMA recommends that the sponsor not be required to re-submit data already available in the sponsor's NDA.

Amending Submitted New Drug Applications – The Guidance is not clear about when sponsors of submitted New Drug Applications should submit proposed amended labeling to include a Geriatric Use subsection. Can an NDA be amended during the review period without re-setting the review clock to add the Geriatric Use subsection information? PhRMA recommends that FDA clarify whether submission of an amended label will modify the user fee completion date for the NDA review.

Timing of Submission of Labeling Supplement – The Guidance, in footnote B to Table 1, states that "If the application holder decides to resume marketing of a drug product, a geriatric labeling supplement should be submitted at or prior to marketing." However, the final rule states that "If an un-marketed approved drug product is subsequently marketed, the product must include appropriate geriatric labeling at the time it is marketed." If the labeling supplement requires prior approval, submission of the supplement "at or prior to marketing" will not enable the sponsor to obtain approval of the label change prior to marketing of the product. PhRMA recommends that FDA clarify that a label supplement that requires prior approval must be submitted before the product is marketed, whether the product is a new product or the sponsor is resuming marketing of an already-approved product.

Timing of Supplement for Priority Marketed Drugs – The Guidance, in Table 2, implies that sponsors of priority drugs for which the NME was first approved prior to August 27, 1998, could have had an impossibly short time period to prepare the required supplement. Yet the final rule stated that those sponsors would have one (1) year in which to prepare the geriatric labeling supplement. FDA should clarify the time allowed for submission of the supplements for these drugs.

Justifying Omission of Geriatric Use Subsection – The Guidance notes that a sponsor can omit the Geriatric Use subsection in a product label if the product is unlikely to be used by the geriatric population. The Guidance does not, however, indicate how a sponsor should justify the omission of a Geriatric Use subsection. PhRMA recommends that FDA clarify the procedure for submission of a justification for omission of the subsection.

PhRMA also notes that the Guidance uses oral contraceptives as an example of a drug class without use in the geriatric population, but oral contraceptives may not be the best example. Although the doses of estrogen/progestin combinations are much lower for oral contraceptives, these combinations are also used in the treatment of osteoporosis, which is prevalent in the geriatric population.

PhRMA would be happy to discuss these comments with FDA staff handling review of geriatric labeling supplements.

Section IV Implementation-
Table 2 "Dates for Submitting Geriatric Labeling"
"labeling" is not a "Type of Submission". Column entry should be "Part of NDA" or "NDA Sections ...." and ... " for example".
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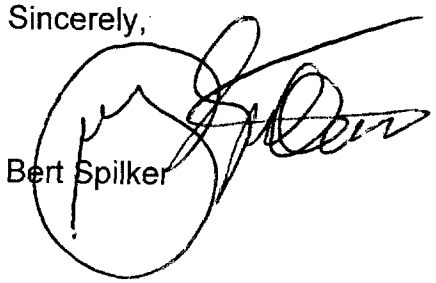
Sincerely,



Bert Spilker